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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/869,122	06/25/01	TANAKA S	064929

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EXAMINER	
HUI, S	

ART UNIT	PAPER NUMBER
1617	5

DATE MAILED: 09/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/869,122	TANAKA ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- Th MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

The amendment filed September 24, 2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

In page 2, last line of the amendment the applicants change the preferred oral dosage to "6 to 9 **mg**". However, in the originally filed specification, page 14, the first paragraph, line 3, discloses the preferred oral dosage herein to be "from about 6 to 9 **mg/kg**". There is a very significant dosage different between "from about 6 to 9 **mg/kg**" and "6 to 9 **mg**", which by no mean, minor amendments as asserted by the applicants.

In page 3, second paragraph, line 2 of the amendment the applicants change the preferred intravenous dosage to "0.5 to 2 **mg**". However, in the originally filed specification, page 14, the second paragraph, line 3, discloses the preferred intravenous dosage herein to be "from about 0.5 to 2 **mg/kg**". There is a very significant dosage different between "from about 0.5 to 2 **mg/kg**" and "0.5 to 2 **mg**", which by no mean, minor amendments as asserted by the applicants.

Applicant is required to cancel the new matter in the reply to this Office Action.

Warning

Applicant is advised that should claim 1 be found allowable, claim 3 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both

cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant is advised that should claim 2 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Please note that the recitations of intended use, e.g., treating bone lesions in multiple myeloma, do not lend patentable weight to the composition claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid and its salts, does not reasonably provide enablement for other active compounds employing in pharmaceutical composition for the treatment of multiple myeloma. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence of absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art
7) the predictability of the art, and
8) the breadth of the claims.

Applicant fails to set forth the criteria that defines an "active ingredient a compound having both an effect of suppressing bone resorption accompanying multiple myeloma and an effect of inhibiting multuiple myeloma". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "active ingredient a compound having both an effect of suppressing bone resorption accompanying multiple myeloma and an effect of inhibiting multuiple myeloma" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "active compounds having both an effect of suppressing bone resorption accompanying multiple myeloma

and an effect of inhibiting multuiple myeloma", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "active ingredient a compound having both an effect of suppressing bone resorption accompanying multiple myeloma and an effect of inhibiting multuiple myeloma" renders the claims indefinite because it is unclear what compounds are encompassed by the claims.

Claim 8 is provides for the use of 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 8 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35

U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Shipman et al. (Leukemia and Lymphoma 1998;32(1-2):129-138 from the Information Disclosure Statement received September 20, 2001).

Shipman et al. teaches that pharmaceutical composition comprising pamidronate for the treatment of multiple myeloma (See particularly page 131, Table 1).

Claims 2, 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Isomura et al. (US Patent 4,990,503 from the Information Disclosure Statement received September 20, 2001).

Isomura et al. teaches a tablet containing 5mg of 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid (See col. 11, line 33-48)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isomura et al. (US Patent 4,990,503 from the Information Disclosure Statement received September 20, 2001) over Shipman et al. (Leukemia and Lymphoma 1998;32(1-2):129-138 from the Information Disclosure Statement received September 20, 2001).

Isomura et al. teaches the heterocyclic bisphosponic acid compounds, including 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, can be blended with other pharmaceutically acceptable carrier to form medical composition suitable for oral administration (See particularly Col. 7, line 7-19; col. 9, example 5).

Isomura et al. does not expressly teach 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid is useful in a method of treating bone lesion in multiple myeloma.

Shipman et al. teaches that potent bisphosphonate, such as clodronate and pamidronate are useful in treating multiple myeloma (See particularly page 131, table 1; page 135, col. 2, conclusion). Shipman et al. teaches that a heterocyclic bisphosphonate, residronate, has a relative potency of 5000 (See page 131, figure 1).

It would have been obvious to one skill in the art when the invention was made to employ 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid in a method of treating bone lesions in multiple myeloma.

One of ordinary skill in the art would have motivated to employ 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid in a method of treating bone lesions in multiple myeloma because it is known that certain potent bisphosphonates are useful in treating multiple myeloma. Therefore, employing any potent bisphosphonates including 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, which its structure is similar to that of residronate, would be reasonably expected to be useful in a method of treating bone lesions in multiple myeloma.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
September 27, 2001

MINNA MOEZIE, J.D.
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